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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Vera Afremova
Art Unit	:	1651
Applicant	:	HART, John Ernest
Serial number	:	09/856,944
Filed	:	July 16, 2001
For	:	Isolated Material Having an Anti-Organotrophic Effect

Assistant Commissioner for Patents
Washington, D. C. 20231

DECLARATION OF DR JOHN ERNEST HART UNDER 37 CFR S. 1.132

1. I am the inventor of the invention described in the above patent application. This Declaration supplements my previous Declaration dated 18 July 2003.

2. I have studied the Office Action sent by the examiner on 13 May 2004. This Declaration is intended to clarify some of the distinctions between the present invention and the cited reference US 4 734 398 (diZerega), which I have read and understood.

3. The compound disclosed by diZerega, "follicular regulating protein" or FRP, does not reduce ovarian mass; exogenous FRP only inhibits the regrowth of juvenile ovaries pre-shrunk by hyophysectomy and then boosted by gonadotropins.

4. What can be predicted to be the likely effect of **endogenous FRP** on ovarian mass in normal intact adults?
Since FRP is only produced in the preovulatory phase, an action at that time only can be posited, and then only on the ovulating ovary, the site of FRP production, no FRP being present in the peripheral circulation. Endogenous gonadotropins increase ovarian mass mid-cycle in adult mammals. Hence, endogenous FRP might blunt this mid-cycle rise in the mass of the ovulating ovary. But there are no grounds for predicting a reduction in the absolute mass of the ovulating ovary or any effect on the mass of the non-ovulating ovary.

5. What if **exogenous FRP** were given to intact adult mammals, rather than hypophysectomised juvenile animals - would that cause an absolute reduction in ovarian mass?
No. All this might achieve would be a blunting of the mid-cycle rise in the mass of the ovulating ovary, given that the mode of action of FRP is to inhibit gonadotropin action. The potential suppression of a rise in mass of the ovulating ovary is not an absolute reduction in the mass of both ovaries, such as can be readily obtained with exogenous micrin.

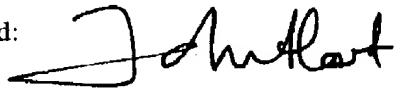
6. Would the administration of **exogenous FRP** to adult intact mammals be expected to cause an absolute reduction in **non-gonadal organ masses**, as is achieved with exogenous micrin?
Again, no. To say otherwise would be to imply that gonadotropins increase the mass of non-

gonadal organs, which is not the case, and ignores the fact that FRP does not even reduce in an absolute sense the mass of an ovulatory ovary; diZerega makes it clear (for example column 11, lines 55-66) that the effect of FRP is to suppress the response to gonadotropins.

7. FRP and micrin are demonstrably separate entities, having no connection whatsoever.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of the application or of any patent issuing thereon.

Further declarant sayeth naught.

Signed: 

Dr John Ernest Hart

Date: 2 August 2004